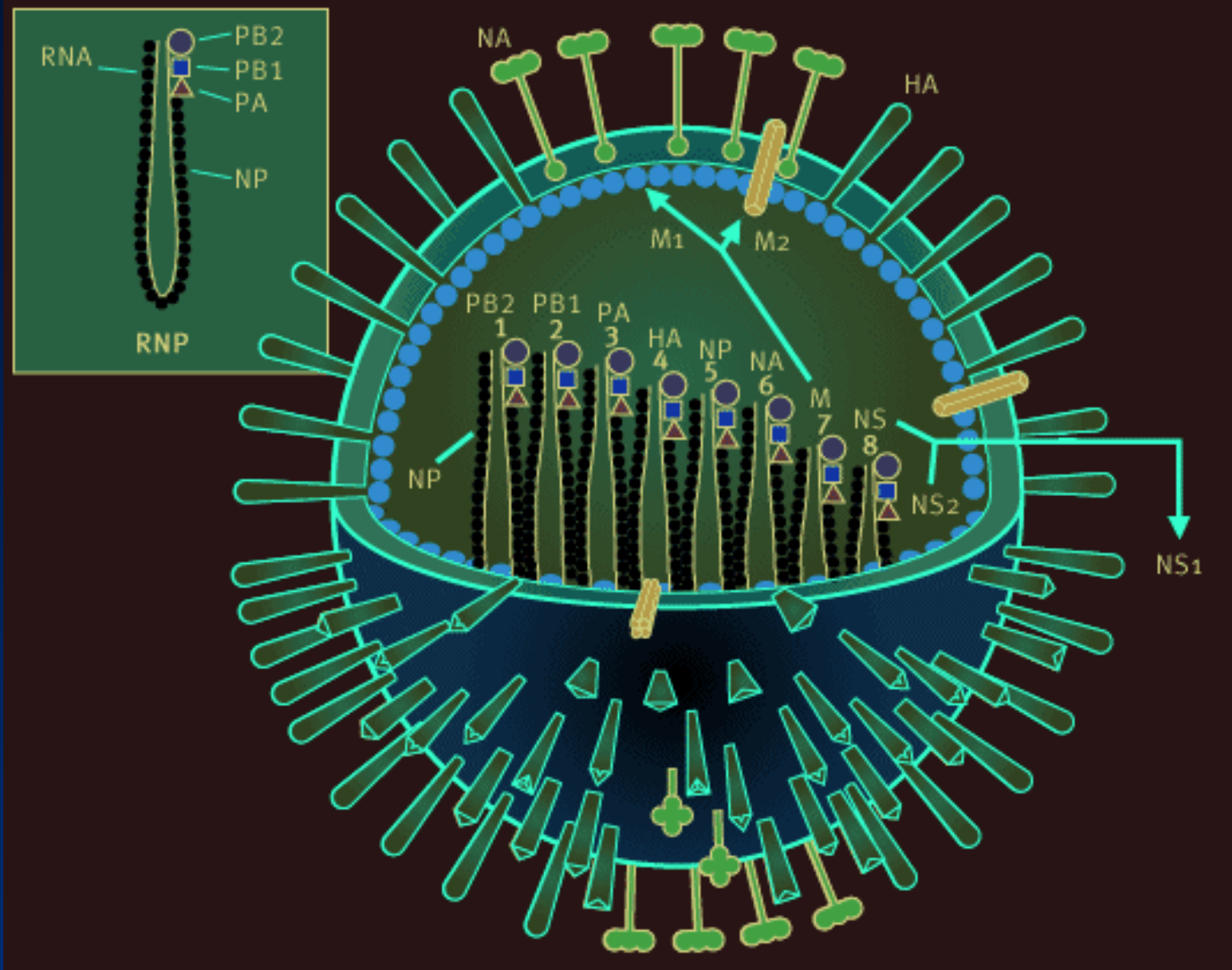


# Influenza:

The Quick Change Artist

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## Influenza A virus



Adapted from Murphy BR et al. In: Fields BN et al, eds. *Fields Virology*. 1996, with permission.

# Influenza Virus

---

## Characteristics

- Myxovirus group



- high infectivity
  - ◆ shortly before symptoms
  - ◆ ends shortly after pyrexia

---

Mandal BK et al. *Lecture Notes on Infectious Diseases*. 1996.

Public Health Image Library. Available at: <http://phil.cdc.gov/phil/home.asp>. Keyword: 1841.  
Accessed November 9, 2006.

# Influenza Virus

---

## Characteristics

- Myxovirus group



- high infectivity
- attack rates up to 5-20%

---

Centers for Disease Control and Prevention. Key facts about influenza and influenza vaccine. August 30, 2006. Available at: [www.cdc.gov/flu/keyfacts.htm](http://www.cdc.gov/flu/keyfacts.htm). Accessed January 16, 2007.  
Public Health Image Library. Available at: <http://phil.cdc.gov/phil/home.asp>. Keyword: 1841.  
Accessed November 9, 2006.

# Influenza Virus

---

## Characteristics

- Myxovirus group



- high infectivity
- attack rates up to 5-20%
- subclinical infection common

---

Centers for Disease Control and Prevention. Key facts about influenza and influenza vaccine. August 30, 2006. Available at: [www.cdc.gov/flu/keyfacts.htm](http://www.cdc.gov/flu/keyfacts.htm). Accessed January 16, 2007.

Mandal BK et al. *Lecture Notes on Infectious Diseases*. 1996.

Public Health Image Library. Available at: <http://phil.cdc.gov/phil/home.asp>. Keyword: 1841. Accessed November 9, 2006.

# Influenza Virus

---

## Characteristics

- Myxovirus group



- high infectivity
- attack rates up to 5-20%
- subclinical infection common
- transmission
  - ◆ infected droplets
  - ◆ contact with contaminant

---

Centers for Disease Control and Prevention. Key facts about influenza and influenza vaccine. August 30, 2006. Available at: [www.cdc.gov/flu/keyfacts.htm](http://www.cdc.gov/flu/keyfacts.htm). Accessed January 16, 2007.

Mandal BK et al. *Lecture Notes on Infectious Diseases*. 1996.

Public Health Image Library. Available at: <http://phil.cdc.gov/phil/home.asp>. Keyword: 1841. Accessed November 9, 2006.

# Influenza Virus

---

## Characteristics

- Myxovirus group



- high infectivity
- attack rates up to 5-20%
- subclinical infection common
- transmission
- cytopathic to respiratory tract

---

Centers for Disease Control and Prevention. Key facts about influenza and influenza vaccine. August 30, 2006. Available at: [www.cdc.gov/flu/keyfacts.htm](http://www.cdc.gov/flu/keyfacts.htm). Accessed January 16, 2007.

Mandal BK et al. *Lecture Notes on Infectious Diseases*. 1996.

Public Health Image Library. Available at: <http://phil.cdc.gov/phil/home.asp>. Keyword: 1841. Accessed November 9, 2006.

# Influenza Virus

---

## Characteristics

- Myxovirus group



- high infectivity
- attack rates up to 5-20%
- subclinical infection common
- transmission
- cytopathic to respiratory tract
- viral characteristics
  - ♦ genome: 8 RNA fragments
  - ♦ nucleocapsid, lipid envelope
  - ♦ two surface antigen proteins
    - hemagglutinin
    - neuraminidase

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Centers for Disease Control and Prevention. Key facts about influenza and influenza vaccine. August 30, 2006. Available at: [www.cdc.gov/flu/keyfacts.htm](http://www.cdc.gov/flu/keyfacts.htm). Accessed January 16, 2007.

Mandal BK et al. *Lecture Notes on Infectious Diseases*. 1996.

Potter CW. In: Zuckerman A et al, eds. *Principles and Practice of Clinical Virology*. 2004.

Public Health Image Library. Available at: <http://phil.cdc.gov/phil/home.asp>. Keyword: 1841. Accessed November 9, 2006.



# Influenza Virus

---

## Characteristics

- Myxovirus group



- high infectivity
- attack rates up to 5-20%
- subclinical infection common
- transmission
- cytopathic to respiratory tract
- viral characteristics
- viral mutation
  - ◆ antigenic drift
    - small continuous change
  - ◆ antigenic shift
    - major sudden change

---

Centers for Disease Control and Prevention. Key facts about influenza and influenza vaccine. August 30, 2006. Available at: [www.cdc.gov/flu/keyfacts.htm](http://www.cdc.gov/flu/keyfacts.htm). Accessed January 16, 2007.

Mandal BK et al. *Lecture Notes on Infectious Diseases*. 1996.

Potter CW. In: Zuckerman A et al, eds. *Principles and Practice of Clinical Virology*. 2004.

Public Health Image Library. Available at: <http://phil.cdc.gov/phil/home.asp>. Keyword: 1841. Accessed November 9, 2006.

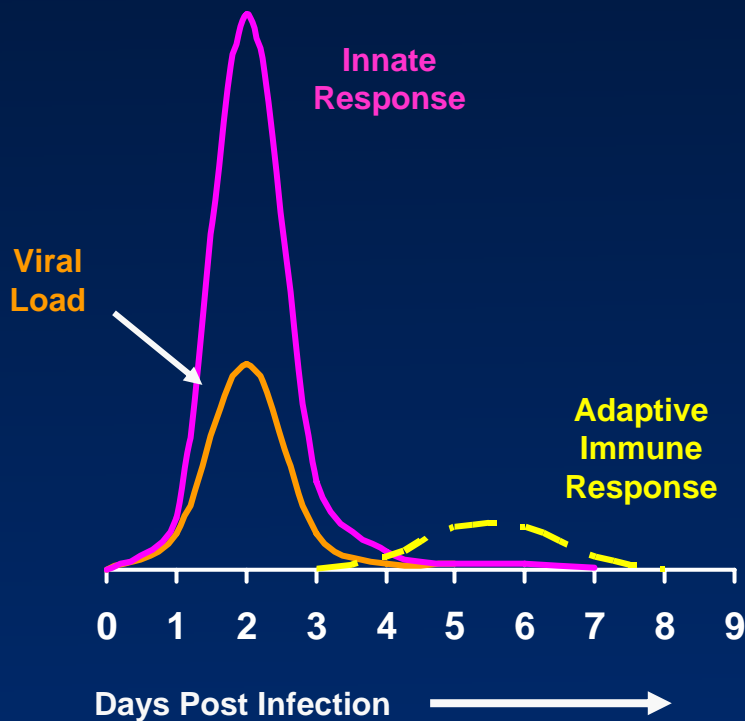
# Influenza Virus



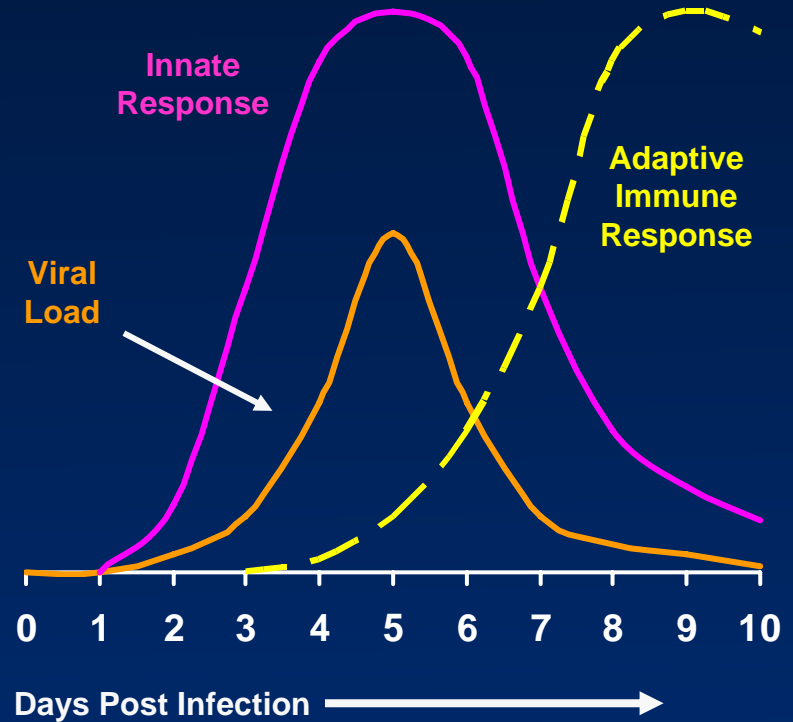
Public Health Image Library. Available at: <http://phil.cdc.gov/PHIL/home.asp>  
Keyword: 8430. Accessed August 18, 2006.

# Immune Response

## Comparative Immune Response



Common Cold



Influenza

Ada G. In: Plotkin SA et al, eds. *Vaccines*. 4<sup>th</sup> ed. 2004.

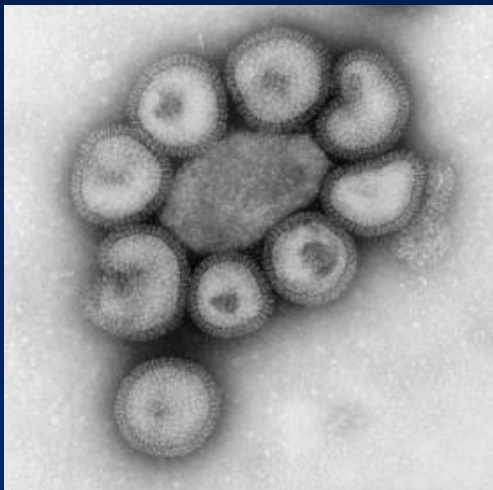
Treanor JJ. In: Mandell GL et al, eds. *Mandell, Douglas, and Bennett's Principles and Practice of Infectious Diseases*. 2005.

# Influenza Virus

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## Characteristics

- Myxovirus group
  - influenza A
    - ♦ affects all age groups
  - moderate to severe illness



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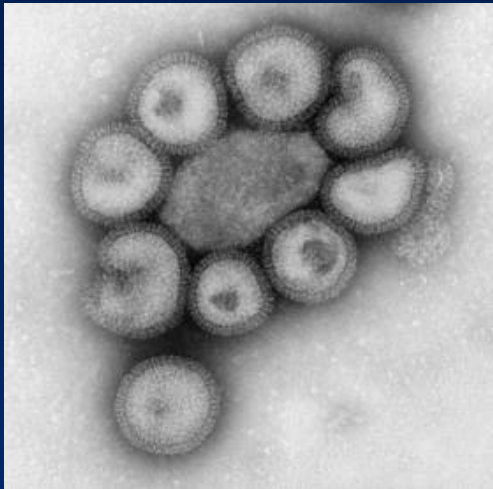
Centers for Disease Control and Prevention. In: Atkinson W et al, eds. *Epidemiology and Prevention of Vaccine-Preventable Diseases*. 2006. Dolin R. In: Braunwald E et al, eds. *Harrison's Principles of Internal Medicine*. 2001. Mandal BK et al. *Lecture Notes on Infectious Diseases*. 1996. Public Health Image Library. Available at: <http://phil.cdc.gov/phil/home.asp>. Keyword: 8432. Accessed November 10, 2006.

# Influenza Virus

---

## Characteristics

- Myxovirus group
  - influenza A
    - ♦ affects all age groups
  - moderate to severe illness
  - epidemics
    - ♦ about every 1-3 years



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Dolin R. In: Braunwald E et al, eds. *Harrison's Principles of Internal Medicine*. 2001.

Mandal BK et al. *Lecture Notes on Infectious Diseases*. 1996.

Public Health Image Library. Available at: <http://phil.cdc.gov/phil/home.asp>. Keyword: 8432.

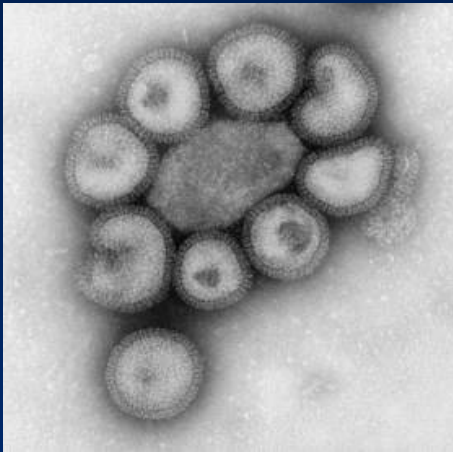
Accessed November 10, 2006.

# Influenza Virus

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## Characteristics

- Myxovirus group
  - influenza A
    - ♦ affects all age groups
    - ♦ Epi/pandemics
  - moderate to severe illness
  - epidemics
    - ♦ about every 1-3 years
  - pandemics
    - ♦ about every 1-2 decades
      - 1890 – H2N2 (Asiatic Flu)
      - 1918 – H1N1 (Spanish Flu)
      - 1957 – H2N2 (Asian Flu)
      - 1968 – H3N2 (Hong Kong Flu)
      - 1976 – H1N1 (Swine Flu Scare)
      - 1977 – H1N1 (Russian Flu Scare)
      - 1997 – H5N1 (Avian Flu Scare)



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Dolin R. In: Braunwald E et al, eds. *Harrison's Principles of Internal Medicine*. 2001.

Mandal BK et al. *Lecture Notes on Infectious Diseases*. 1996.

Murphy BR et al. In: Fields BN et al, eds. *Fields Virology*. 1996.

Public Health Image Library. Available at: <http://phil.cdc.gov/phil/home.asp>. Keyword: 8432.

Accessed November 10, 2006.

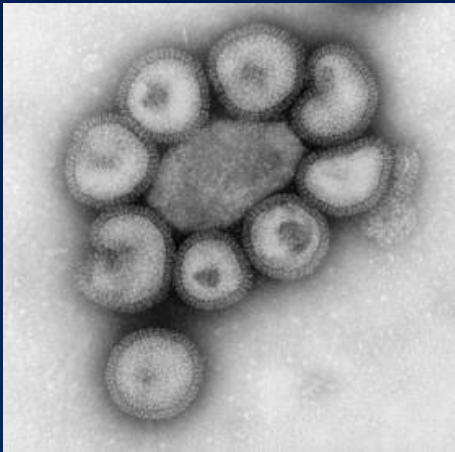
US Department of Health & Human Services. Available at: <http://www.hhs.gov/nvpo/pandemics/flu3.htm>. Accessed April 17, 2006.

# Influenza Virus

---

## Characteristics

- Myxovirus group
  - influenza A
    - ♦ affects all age groups
    - ♦ epi/pandemics
  - moderate to severe illness
  - epidemics
    - ♦ every 1-3 years
  - pandemics
    - ♦ every 1-2 decades
  - influenza A mutation
    - ♦ antigenic drift
      - small continuous change
      - RNA point mutations



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Air GM et al. *Proc Natl Acad Sci USA*. 1990;87:3884-3888.

Dolin R. In: Braunwald E et al, eds. *Harrison's Principles of Internal Medicine*. 2001.

Mandal BK et al. *Lecture Notes on Infectious Diseases*. 1996.

Potter CW. In: Zuckerman A et al, eds. *Principles and Practice of Clinical Virology*. 2004.

Public Health Image Library. Available at: <http://phil.cdc.gov/phil/home.asp>. Keyword: 8432.

Accessed November 10, 2006.

# Influenza Virus

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## Characteristics

- Myxovirus group
  - influenza A
    - ◆ affects all age groups
    - ◆ epi/pandemics
    - ◆ antigenic drift/shift
  - moderate to severe illness
  - epidemics
    - ◆ every 1-3 years
  - pandemics
    - ◆ every 1-2 decades
  - influenza A mutation
    - ◆ antigenic drift
    - ◆ antigenic shift
      - major sudden change
      - exchange of genes in animal reservoir

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Dolin R. In: Braunwald E et al, eds. *Harrison's Principles of Internal Medicine*. 2001.

Mandal BK et al. *Lecture Notes on Infectious Diseases*. 1996.

Potter CW. In: Zuckerman A et al, eds. *Principles and Practice of Clinical Virology*. 2004.



# Influenza Virus

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## Characteristics

- Myxovirus group
  - influenza B
    - causes relatively few cases
      - ♦ sporadic infections

---

Centers for Disease Control and Prevention. In: Atkinson W et al, eds. *Epidemiology and Prevention of Vaccine-Preventable Diseases*. 2006.

Dolin R. In: Braunwald E et al, eds. *Harrison's Principles of Internal Medicine*. 2001.

Mandal BK et al. *Lecture Notes on Infectious Diseases*. 1996.

# Influenza Virus

---

## Characteristics

- Myxovirus group
  - influenza B
    - causes relatively few cases
    - local epidemics
      - ♦ about every 2 years

---

Centers for Disease Control and Prevention. In: Atkinson W et al, eds. *Epidemiology and Prevention of Vaccine-Preventable Diseases*. 2006.

Mandal BK et al. *Lecture Notes on Infectious Diseases*. 1996.

# Influenza Virus

---

## Characteristics

- Myxovirus group
  - influenza B
    - causes relatively few cases
    - local epidemics
      - ♦ about every 2 years
    - especially children

# Influenza Virus

---

## Characteristics

- Myxovirus group
  - influenza B
    - causes relatively few cases
    - local epidemics
      - ♦ about every 2 years
    - especially children
    - influenza B mutation
      - ♦ antigenic drift
        - small continuous change
        - RNA point mutations

---

Air GM et al. *Proc Natl Acad Sci USA*. 1990;87:3884-3888.

Dolin R. In: Braunwald E et al, eds. *Harrison's Principles of Internal Medicine*. 2001.

Mandal BK et al. *Lecture Notes on Infectious Diseases*. 1996.

Potter CW. In: Zuckerman A et al, eds. *Principles and Practice of Clinical Virology*. 2004.

# Influenza Virus

---

## Characteristics

- Myxovirus group
  - influenza B
    - ♦ antigenic drift
  - causes relatively few cases
  - local epidemics
    - ♦ about every 2 years
  - especially children
  - influenza B mutation
    - ♦ antigenic drift
      - small continuous change
      - error prone RNA polymerase
    - ♦ antigenic shift
      - ~~no antigenic shift~~

---

Dolin R. In: Braunwald E et al, eds. *Harrison's Principles of Internal Medicine*. 2001.

Potter CW. In: Zuckerman A et al, eds. *Principles and Practice of Clinical Virology*. 2004.

# Influenza Virus

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## Characteristics

- Myxovirus group
  - influenza C
  - rarely causes human disease

---

Centers for Disease Control and Prevention. In: Atkinson W et al, eds. *Epidemiology and Prevention of Vaccine-Preventable Diseases*. 2006.

Dolin R. In: Braunwald E et al, eds. *Harrison's Principles of Internal Medicine*. 2001.

Potter CW. In: Zuckerman A et al, eds. *Principles and Practice of Clinical Virology*. 2004.

# Cytokine Involvement

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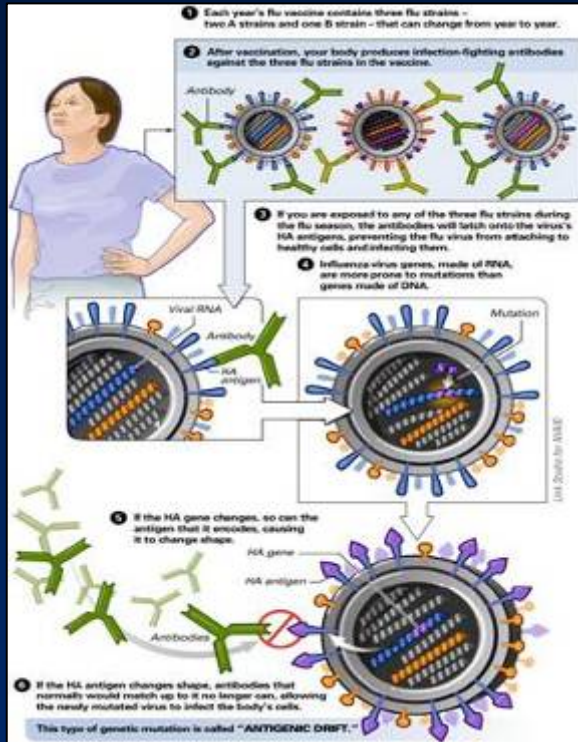
- Influenza infection is localized within the respiratory tract, but the release of cytokines is associated with systemic symptoms and host defenses
- IL-6 and IFN- $\alpha$  are the primary cytokines associated with influenza symptoms
- IL-6 appears to play a major role in symptom formation
- IFN-  $\alpha$  induces NK cell activity
  - NK cells limit viral infection until the host mounts a primary antigen-specific B or T cell response

---

Hayden FG et al. *J Clin Invest.* 1998;101:643-649.

# Influenza Virus

## Characteristics



### – antigenic drift

- small continuous change
  - accumulation of point mutations
- ◆ influenza is an RNA virus
  - ◆ error prone RNA polymerase
    - can not proofread its work
    - A: 1 error / 10,000 base pairs
    - B: 1 error / 1,000,000 base pairs
  - ◆ human DNA polymerase
    - can proofread its work
    - 1 error / 1 billion base pairs

Air GM et al. *Proc Natl Acad Sci USA*. 1990;87:3884-3888.

Mandal BK et al. *Lecture Notes on Infectious Diseases*. 1996.

National Institute of Allergy and Infectious Diseases. Available at: <http://www3.niaid.nih.gov/news/focuson/flu/illustrations/antigenic/antigenicdrift.htm>. Accessed October 31, 2006.

Potter CW. In: Zuckerman A et al, eds. *Principles and Practice of Clinical Virology*. 2004.

Replication. Available at: [http://www.bookrags.com/research/replication-gen\\_04.html](http://www.bookrags.com/research/replication-gen_04.html). Accessed October 31, 2006.



# Influenza Virus

## Characteristics

- antigenic shift

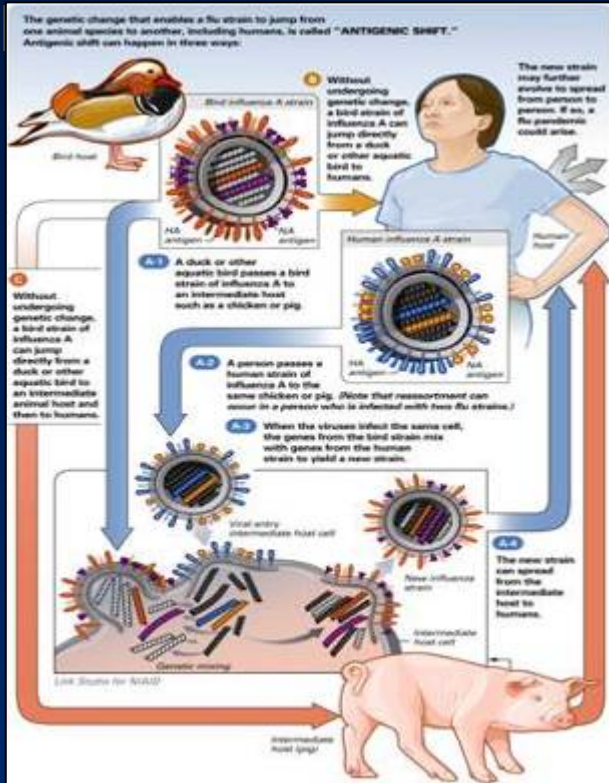
- major sudden change
- exchange of genes in animal reservoir

- ◆ influenza A is an RNA virus

- genome of 8 separate fragments
- avian influenza infects swine
- human influenza infects swine
- swine is a mixing pot for fragments

- ◆ new virus with 8 RNA fragments

- 6 fragments may be human origin
- 2 fragments may be avian origin



National Institute of Allergy and Infectious Diseases. Available at:  
<http://www3.niaid.nih.gov/news/focuson/flu/illustrations/antigenic/antigenicshift.htm>. Accessed October 31, 2006.

Mandal BK et al. *Lecture Notes on Infectious Diseases*. 1996.

Potter CW. In: Zuckerman A et al, eds. *Principles and Practice of Clinical Virology*. 2004.

# 1918 Pandemic Influenza

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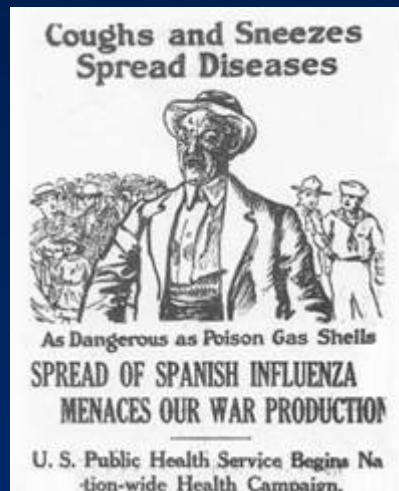
## Philadelphia, Fall of 1918

*“As their lungs filled ... the patients became short of breath and increasingly cyanotic. After gasping for several hours they became delirious and incontinent, and many died struggling to clear their airways of a blood-tinged froth that sometimes gushed from their nose and mouth. It was a dreadful business.”*

Isaac Starr – Third-Year Medical Student

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Starr I. *Ann Intern Med.* 2006;145:138-140.



**THE COST OF THE COMMON COLD & INFLUENZA**

**Think it all the time.**  
 On an average 20 million colds are had in your city each winter.  
 They cost over 10 million people in extra time paid for lost work.  
 They cost over 10 million dollars each year.  
 The death of 50,000 men for one year.

At 17 1/2 million of it, the war and winter also had  
 these things, making today, our last numbers,  
 the same 100 million.

**Keep it that low. Don't spoil it.**

	8,500 TANKS
	1,000 TANKS
	100,000 RIFLES

That is the cost of one war effort. You can all be helped to a cold  
 cure. By your help you can stop the spread of colds. By stopping  
 the spread of colds you can save the war.

**HELP TO KEEP THE NATION FIGHTING HOT**

US Department of the Navy. Available at: <http://www.history.navy.mil/photos/events/ev-1910s/ev-1918/influenz.htm>. Accessed November 10, 2006.

National Archives. Available at: <http://www.archives.gov/exhibits/influenza-epidemics/records-list.html>. Accessed November 13, 2006.

National Library of Medicine. Available at: <http://www.nlm.nih.gov/ihm/images/A/27/712.jpg>. Accessed November 13, 2006.

# 1918 Pandemic Influenza

---

## Morbidity and Mortality

- United States
  - 25 million infected
  - 500,000 died
- England & Wales
  - 200,000 died
- Worldwide
  - 500 million stricken
  - mortality
    - ◆ low: 20 Million
    - ◆ high: 100 Million



---

<sup>1</sup> Mandal BK et al. *Lecture Notes on Infectious Diseases*. 1996.

National Library of Medicine. Available at: <http://www.nlm.nih.gov/ihm/images/A/07/197.jpg>. Accessed November 13, 2006.

National Library of Medicine. Available at: <http://www.nlm.nih.gov/ihm/images/A/06/721.jpg>. Accessed November 13, 2006.

Taubenberger JK et al. *Emerg Infect Dis*. 2006;12:15-22.

<sup>2</sup> US Department of Health & Human Services. Available at:

<http://www.hhs.gov/nvpo/pandemics/index.html>. Accessed April 17, 2006.

# 1918 Pandemic Influenza

---

## Morbidity and Mortality

- United States
  - 500,000 died
- England & Wales
  - 200,000 died
- Worldwide
  - 500 million stricken
  - mortality
    - ♦ low: 20 million
    - ♦ high: 100 million
- Comparison mortality
  - AIDS 25 million (2005)
  - The Great War
    - ♦ approximately 10 million died (combat)
  - World War II
    - ♦ Approximately 25 million died (combat)
- Lethality/mortality
  - 1918: 2.5% of victims
  - normal: 0.1% of victims

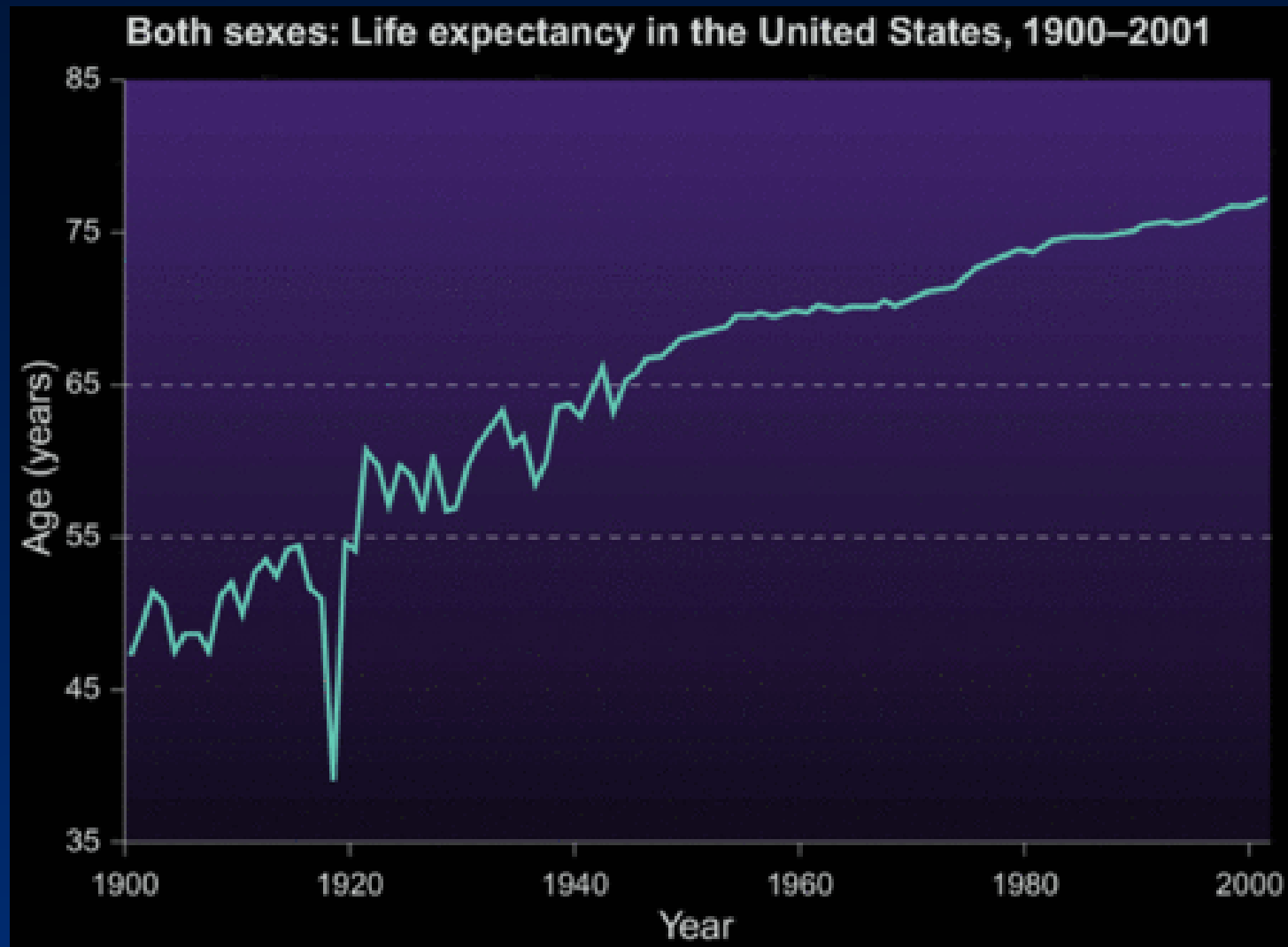
---

Mandal BK et al. *Lecture Notes on Infectious Diseases*. 1996.

Kolata G. *Flu: The Story of the Great Influenza Pandemic of 1918 and the Search for the Virus that Caused It*. 1999.

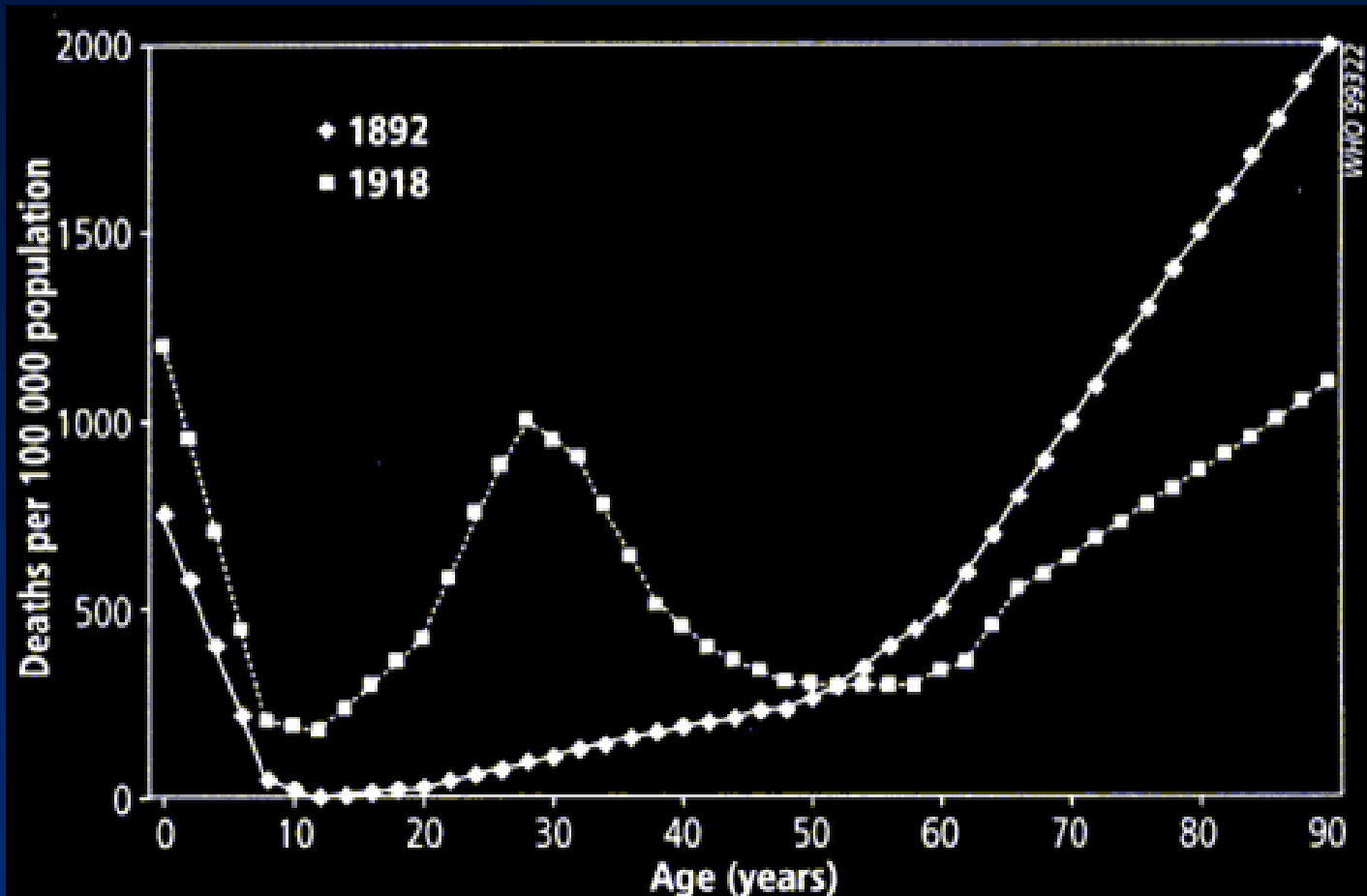
US Department of Health & Human Services. Available at: <http://www.hhs.gov/nvpa/pandemics/index.html>. Accessed October 31, 2006.

# Impact Of 1918 Influenza On Life Expectancy



Palese P. *Nature Medicine*. 2004;10:S82-S87, with permission.

# Pandemic Influenza: Age-Related Mortality



Data for 1892 for Massachusetts only.

Dowdle WR. *Bull World Health Org.* 1999;77:820-828, with permission.

# Comparative Pandemics

## Morbidity And Mortality (USA)

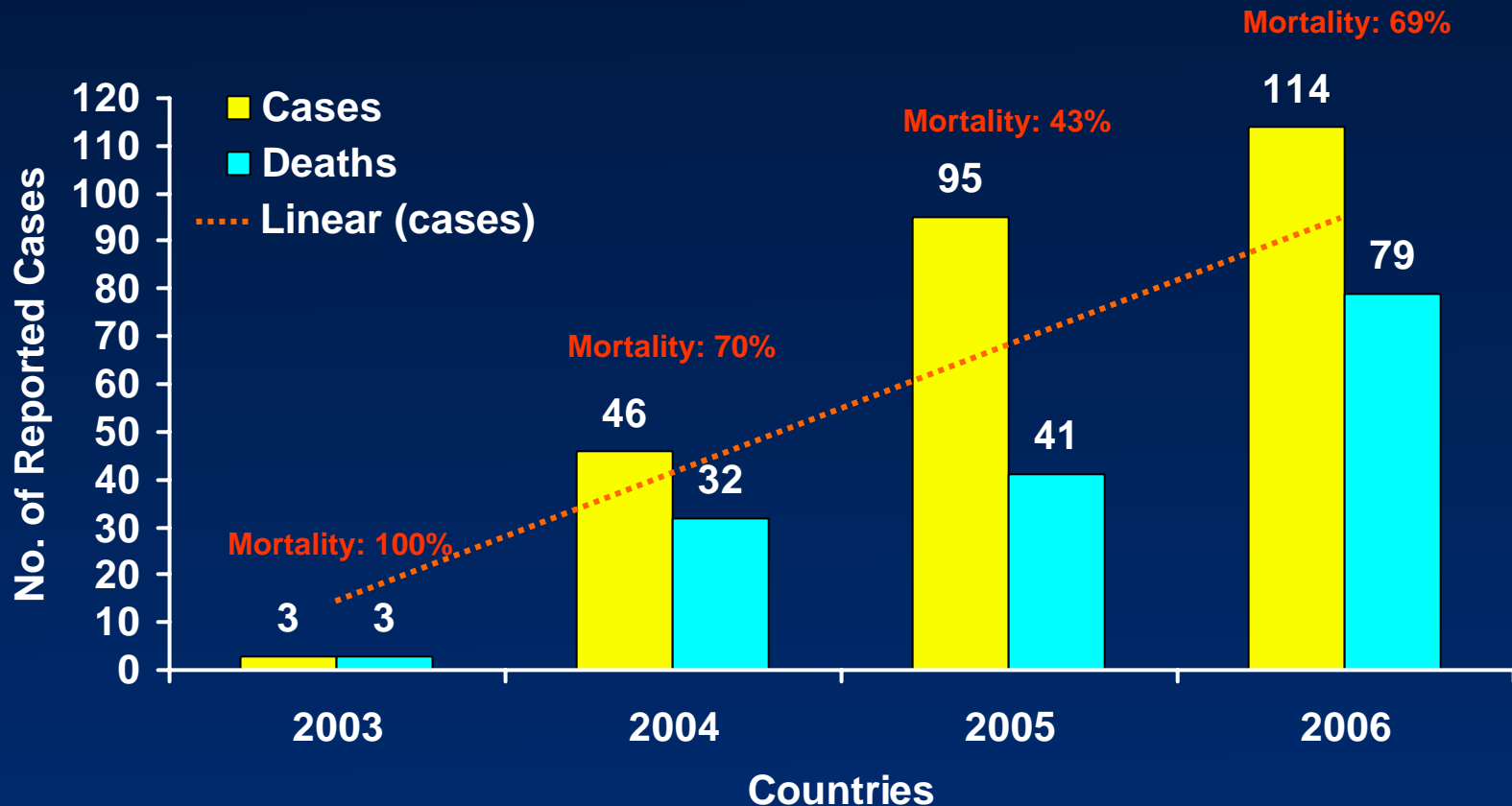
	Moderate 15% Attack Rate	Severe 35% Attack Rate
Illness	38 million	89 million
Outpatient medical care	18 million	42 million
Hospitalization	314,000	734,000
Deaths	89,000	207,000

Meltzer MI et al. *Emerg Infect Dis.* 1999;5:659-671.



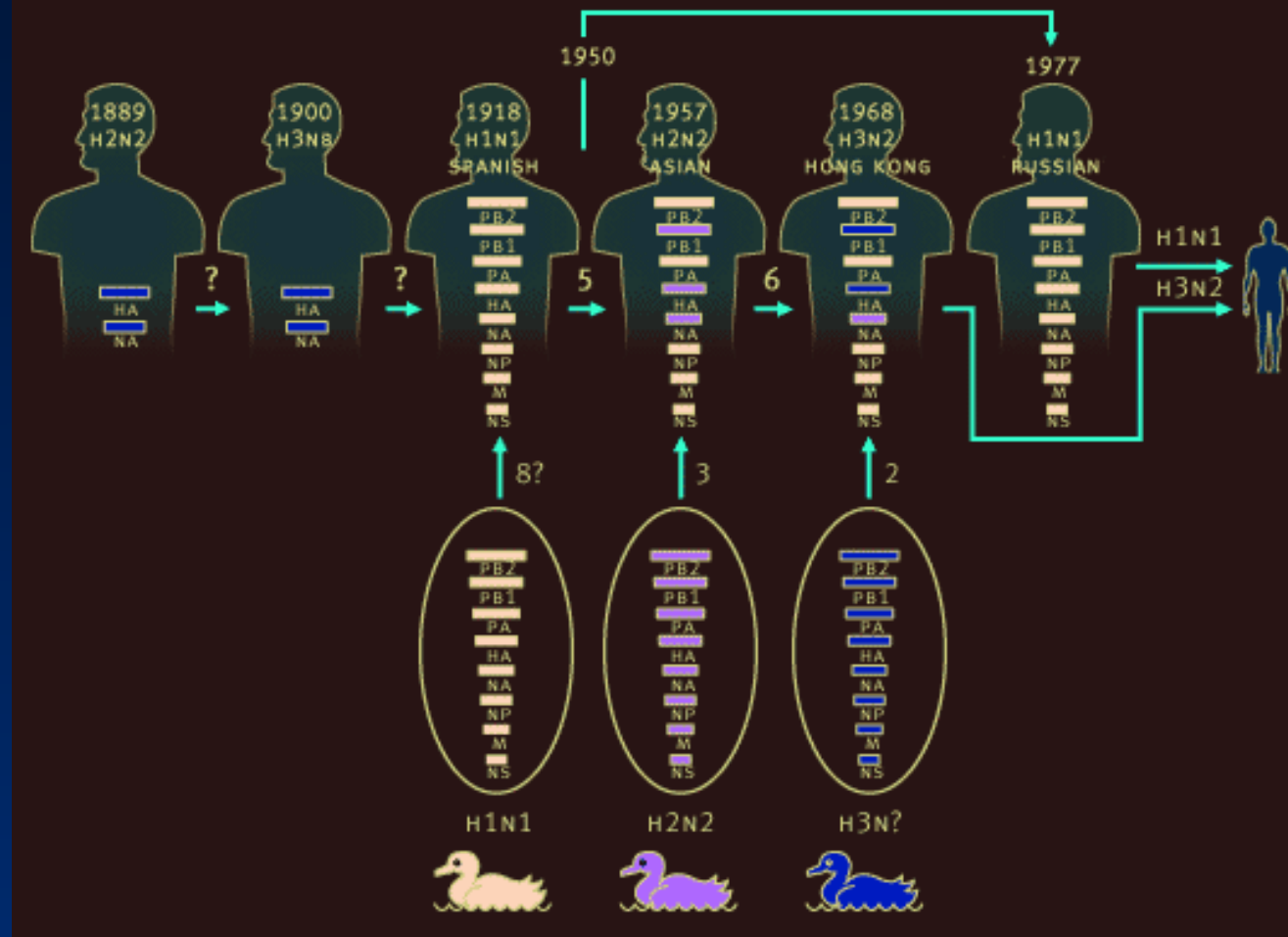
# Comparative Pandemics

## H5N1 (Currently Emerging) Mortality

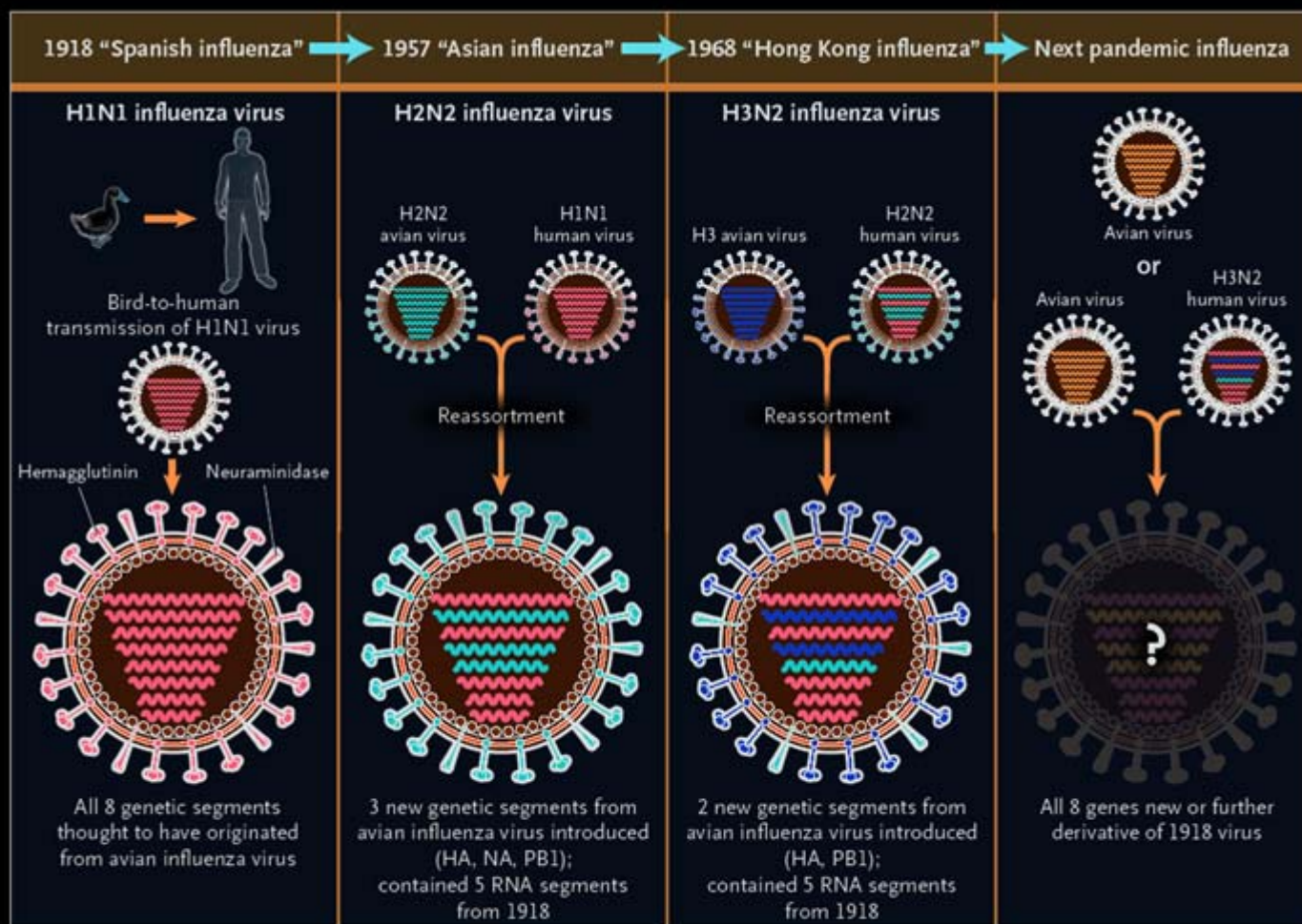


WHO Global Influenza Program. Available at: [http://www.who.int/wor/disease/avian\\_influenza/country/cases\\_table\\_2007\\_01\\_09/en/index.html](http://www.who.int/wor/disease/avian_influenza/country/cases_table_2007_01_09/en/index.html). Accessed January 10, 2007.

## Origin of human pandemic influenza A viruses



Murphy BR et al. In: Fields BN et al, eds. *Fields Virology*. 1996, with permission.



**The Two Mechanisms whereby Pandemic Influenza Originates.**

In 1918, an H1N1 virus closely related to avian viruses adapted to replicate efficiently in humans. In 1957 and in 1968, reassortment events led to new viruses that resulted in pandemic influenza. The 1957 influenza virus (Asian influenza, an H2N2 virus) acquired three genetic segments from an avian species (a hemagglutinin, a neuraminidase, and a polymerase gene, PB1), and the 1968 influenza virus (Hong Kong influenza, an H3N2 virus) acquired two genetic segments from an avian species (hemagglutinin and PB1). Future pandemic strains could arise through either mechanism.

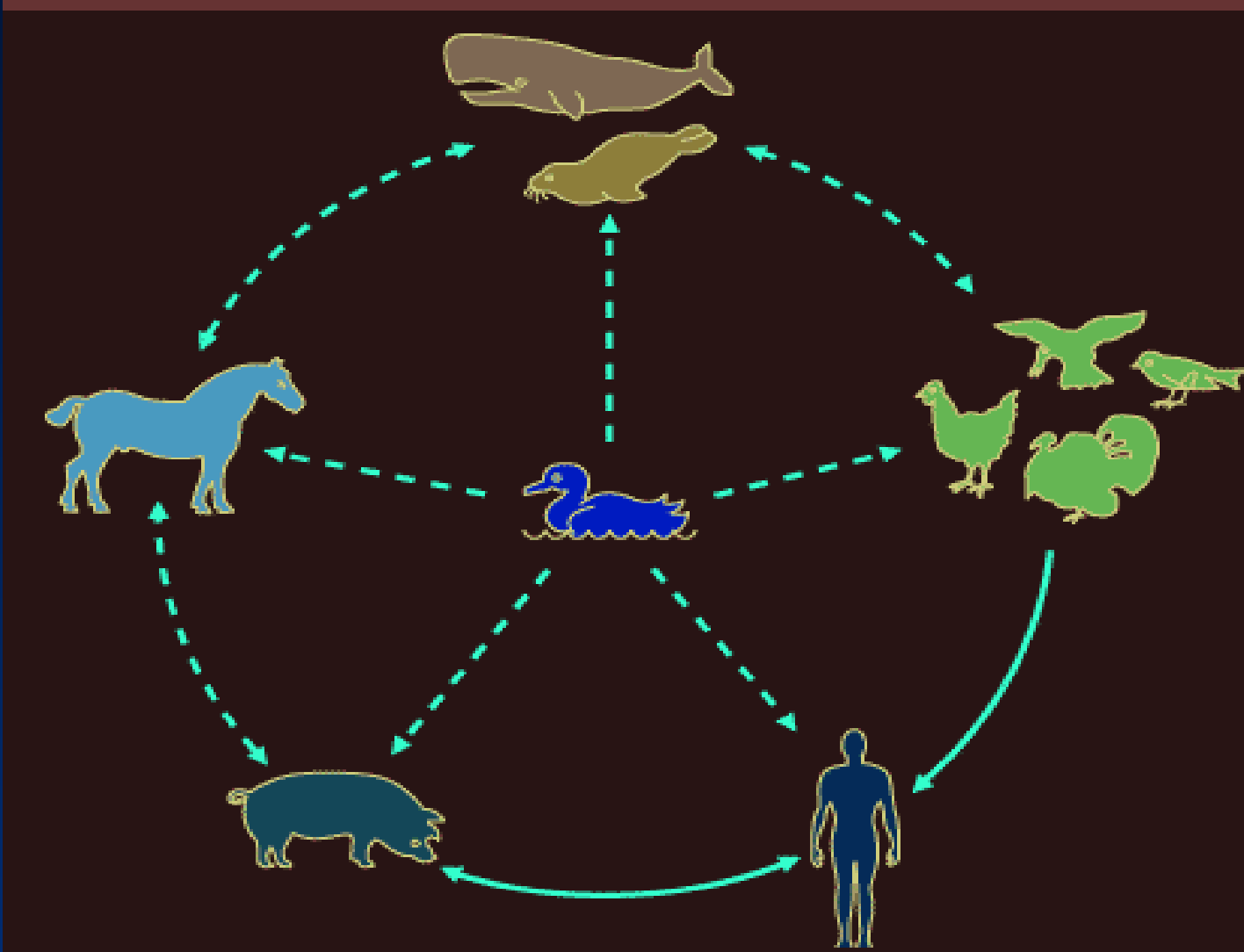
# Natural Hosts Of Influenza Viruses

HA Subtype	Host				NA Subtype	Host			
	Human	Swine	Equine	Avian		Human	Swine	Equine	Avian
H1	✓	✓		✓	N1	✓	✓		✓
H2	✓			✓	N2	✓	✓		✓
H3	✓	✓	✓	✓	N3				✓
H4				✓	N4				✓
H5				✓	N5				✓
H6				✓	N6				✓
H7			✓	✓	N7			✓	✓
H8				✓	N8			✓	✓
H9				✓	N9				✓
H10				✓					
H11				✓					
H12				✓					
H13				✓					
H14				✓					
H15				✓					
H16				✓					

Fouchier RA, et al. *J Virol.* 2005;79:2814-2822.

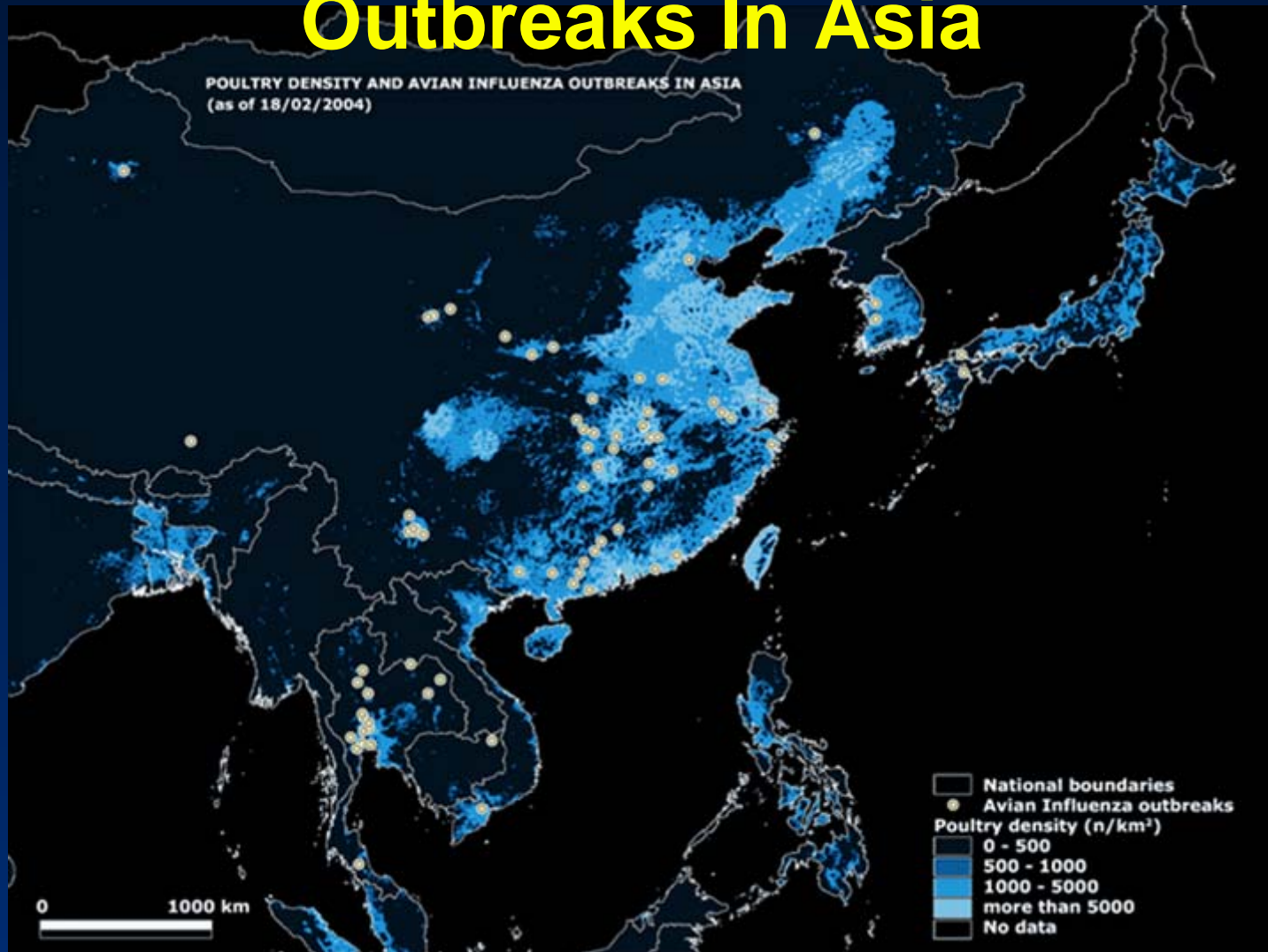
Nicholson KG, et al. *Lancet.* 2003;362:1733-1745.

## The reservoir of influenza A viruses



Murphy BR et al. In: Fields BN et al, eds. *Fields Virology*. 1996, with permission.

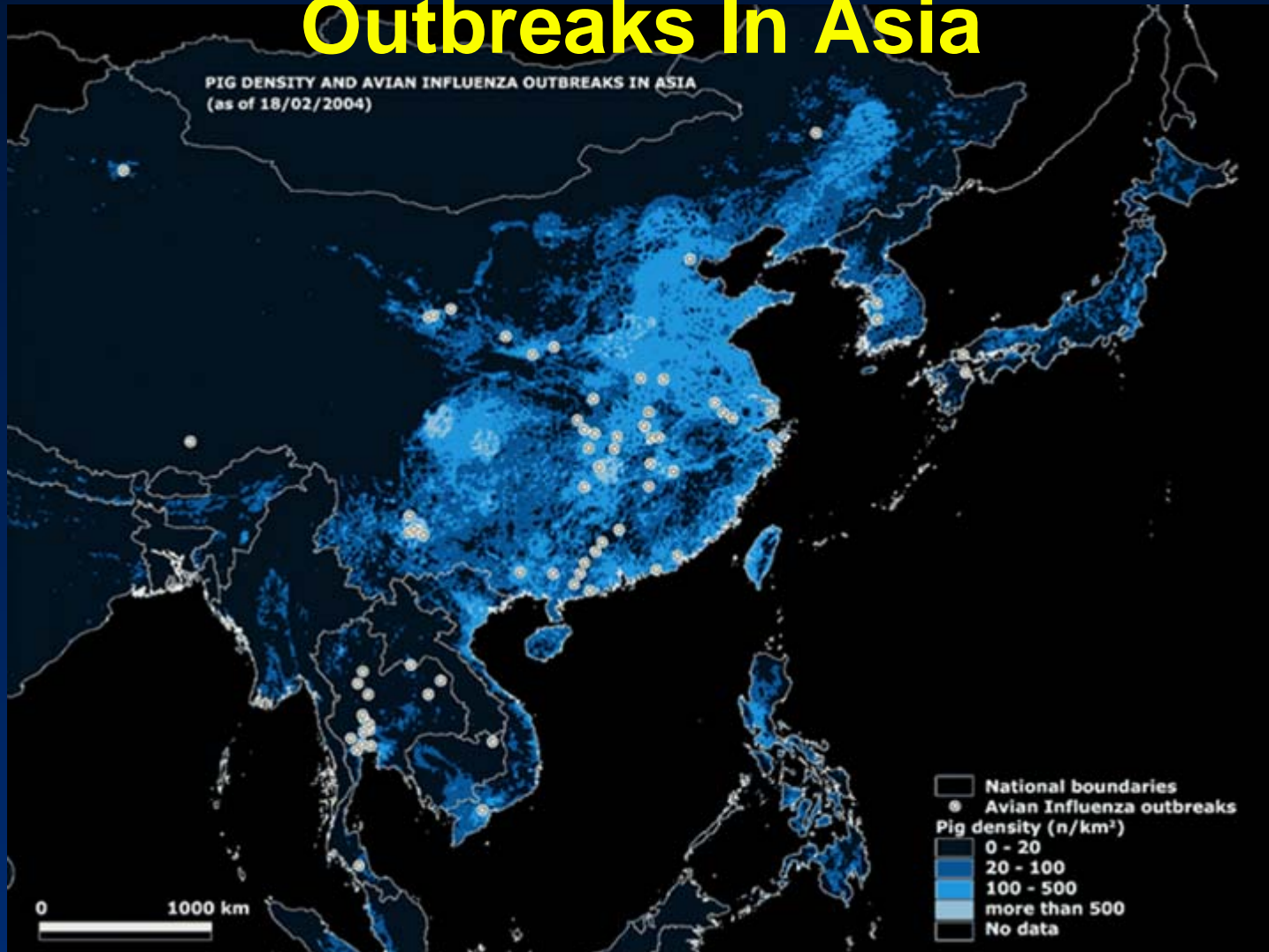
# Poultry Density And Avian Influenza Outbreaks In Asia



Poultry Density and Avian Influenza Outbreaks in Asia. Available at: [http://www.fao.org/ag/aga/agah/empres/Images/avianpoultry180204\\_800x600.gif](http://www.fao.org/ag/aga/agah/empres/Images/avianpoultry180204_800x600.gif). Accessed October 31, 2006.

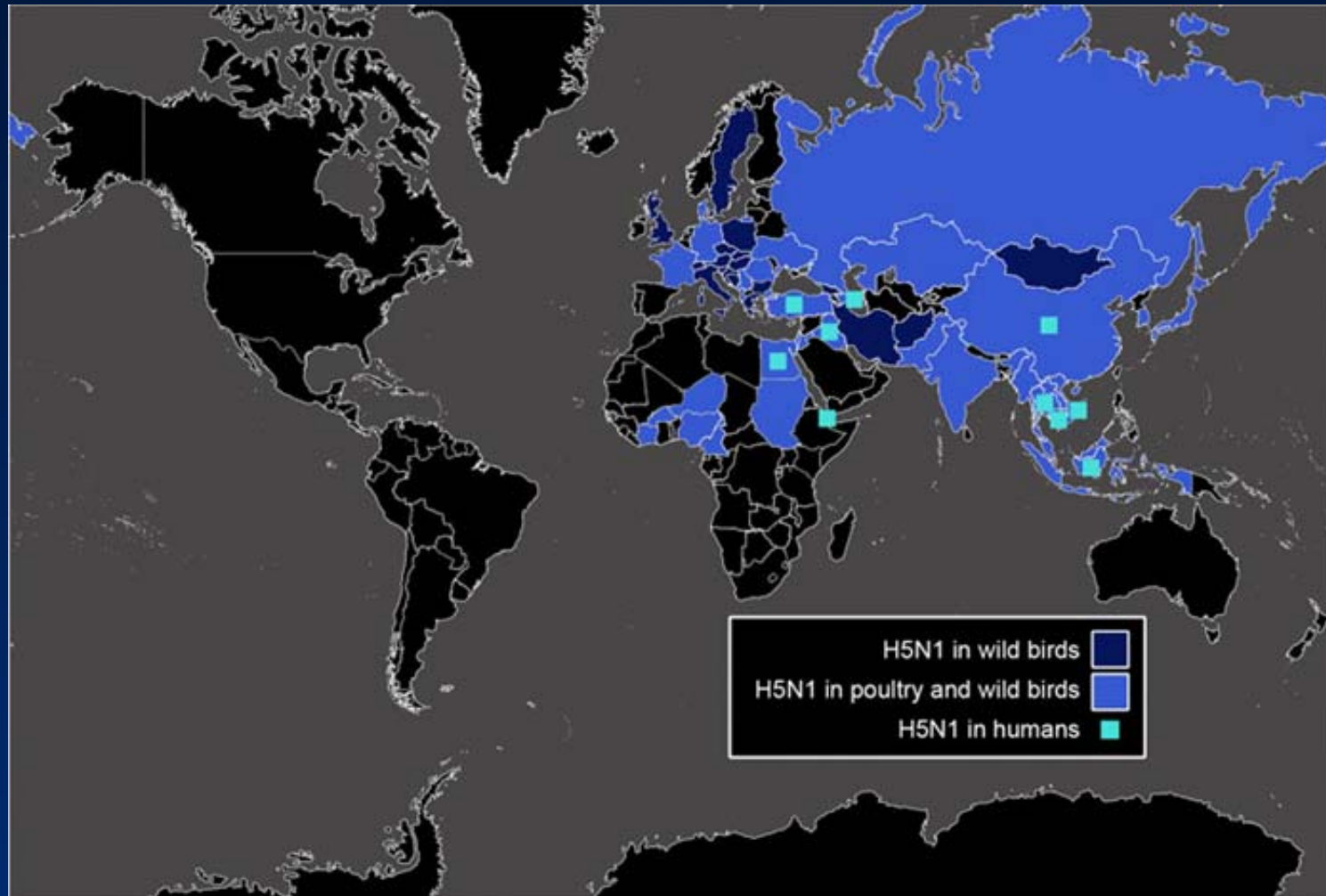


# Pig Density And Avian Influenza Outbreaks In Asia



Pig Density and Avian Influenza Outbreaks in Asia. Available at: [http://www.fao.org/ag/aga/agah/empres/Images/avianoig180204\\_800x600.gif](http://www.fao.org/ag/aga/agah/empres/Images/avianoig180204_800x600.gif). Accessed October 31, 2006.

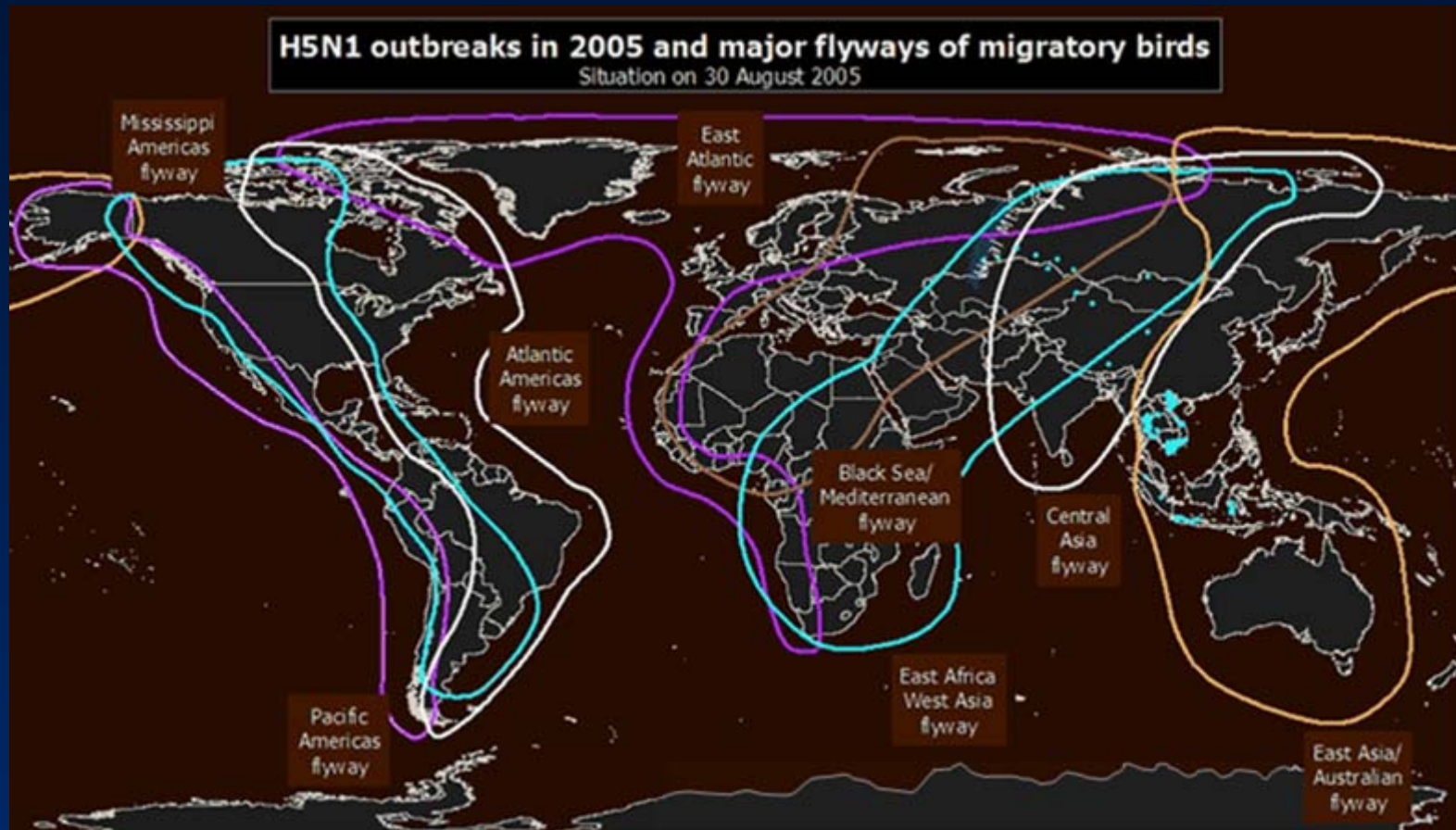
# Emerging Avian Influenza



US Department of Health and Human Services. Available at:  
[http://www.pandemicflu.gov/images/pop\\_Image.jpg](http://www.pandemicflu.gov/images/pop_Image.jpg). Accessed May 19, 2006.



# Migratory Bird Pattern



- Districts with H5N1 outbreaks since January 2005

Reproduced from United Nations Food and Agriculture Organization 2005, with permission. All rights reserved. Compiled by FAO AGAH, EMPRES Programme. Data sources: AI outbreaks: OIE, FAO and Government sources. Flyways: Wetlands International. Food and Agriculture Organization. Available at: <http://www.fao.org/ag/againfo/subjects/en/health/diseases-cards/migrationmap.html>. Accessed March 13, 2006.

# Avian Influenza (Bird Flu) And The H5N1 Virus

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- The avian flu currently of concern is the H5N1 subtype, which is highly pathogenic
  - Many different subtypes of type A influenza viruses exist that vary based on changes in the hemagglutinin and neuraminidase proteins on the surface of the virus
  - The virus that causes avian influenza infection in domestic poultry results in a range in severity of disease
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US Department of Health & Human Services. Available at:  
<http://www.pandemicflu.gov/general/>. Accessed January 10, 2007.

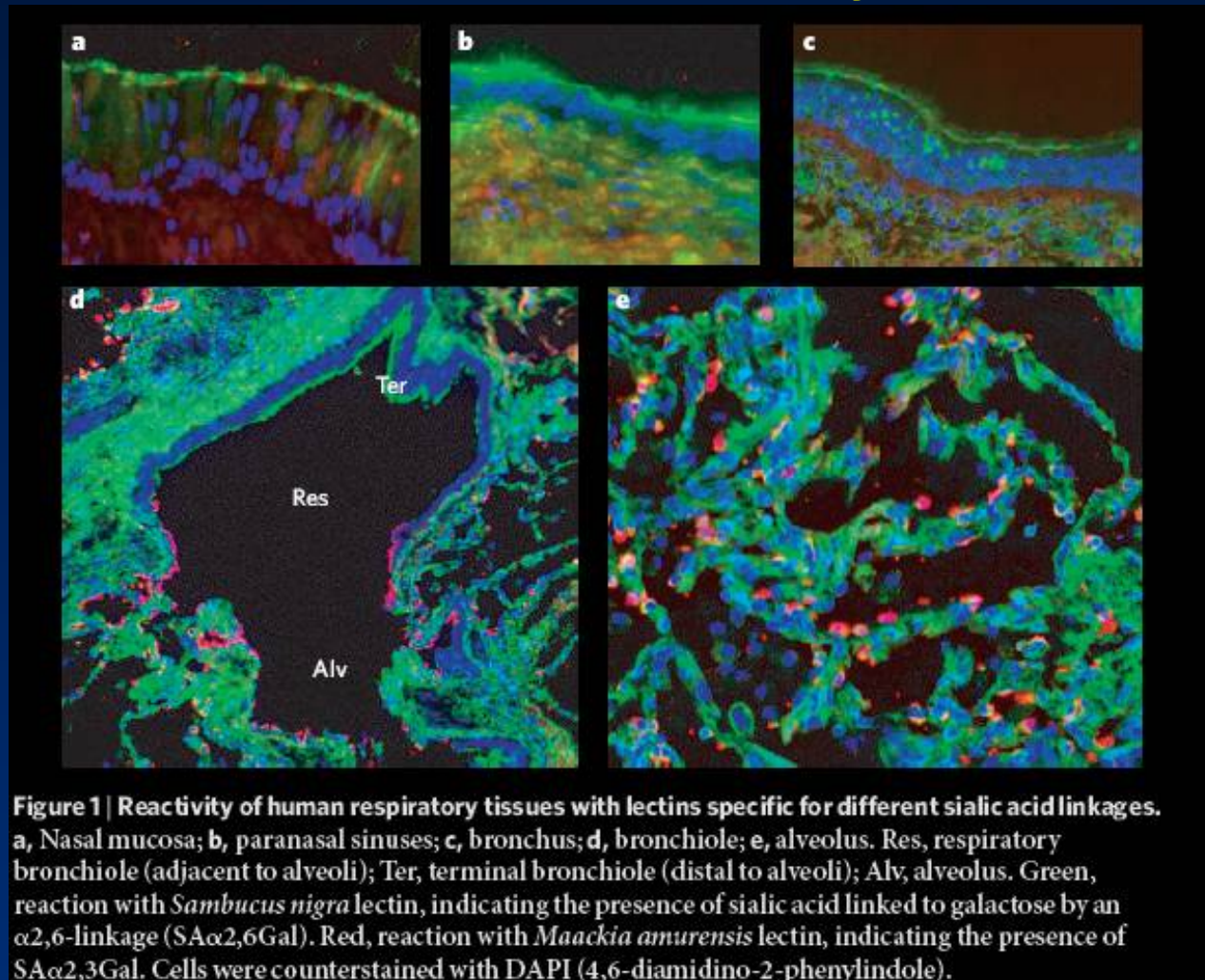
# Human Infection During The H5N1 Outbreak

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- H5N1 is one of the few avian influenza viruses to have crossed the species barrier to infect humans
    - human infection has mostly occurred by direct contact with diseased poultry
  - H5N1 is highly pathogenic
    - in the current outbreaks in Asia and Europe, >50% of those infected with the H5N1 virus have died
  - Most cases have occurred in previously healthy children and young adults
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US Department of Health & Human Services. Available at:  
<http://www.pandemicflu.gov/general/>. Accessed January 10, 2007.

# Influenza Virus Receptors In The Human Respiratory Tract



Shinya K et al. *Nature*. 2006;440:435-436, with permission.

# Pandemic Alert Phases

<b>Inter-Pandemic Phase</b> <b>New Virus in Animals, NO Human Cases</b>	<b>Low Risk of Human Cases</b>	<b>1</b>
	<b>High Risk of Human Cases</b>	<b>2</b>
<b>Pandemic ALERT</b> <b>New Virus Causes Human Cases</b>	<b>No or Very Limited Human-to-Human Transmission</b>	<b>3</b>
	<b>Evidence of Increased Human-to-Human Transmission</b>	<b>4</b>
	<b>Evidence of Significant Human-to-Human Transmission</b>	<b>5</b>
<b>PANDEMIC</b>	<b>Efficient &amp; Sustained Human-to-Human Transmission</b>	<b>6</b>

WHO Global Influenza Program. Current WHO Phase of Pandemic Alert. Available at: [http://www.who.int/csr/disease/avian\\_influenza/phase/en/index.html](http://www.who.int/csr/disease/avian_influenza/phase/en/index.html).



# Pandemic Plan For The Spread Of Avian Influenza

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- Because these viruses do not commonly infect humans, there is little or no immune protection against them in the human population<sup>1</sup>
- If H5N1 virus were to gain the capacity to spread easily from person to person, a pandemic could begin<sup>1</sup>
- The US Department of Health & Human Services (HHS) and other federal agencies are holding pandemic planning summits<sup>2</sup>

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<sup>1</sup> US Department of Health & Human Services. Available at: <http://www.pandemicflu.gov/general/>. Accessed January 10, 2007.

<sup>2</sup> US Department of Health & Human Services. Available at: <http://www.pandemicflu.gov/plan/tab2.html>. Accessed February 24, 2006.

# Pandemic Plan For The Spread Of Avian Influenza

## US Department of Health & Human Services

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- HHS Pandemic Influenza Plan
  - blueprint for pandemic influenza preparation and response
  - goal is to achieve state of readiness and quick response
  - US will work with WHO and other international partners
- Major component for preparedness includes stockpiling of antivirals and vaccines
  - production capacity to provide vaccine for entire US population
  - quantities of antiviral drugs sufficient to treat 25% of US population

# Other Emerging Influenza A Viruses

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- H7N2<sup>1</sup>
  - ◆ New York
- H7N3<sup>1</sup>
  - ◆ Canada
- H7N7<sup>2</sup>
  - ◆ United Kingdom
  - ◆ Netherlands
- H9N2<sup>2</sup>
  - ◆ Hong Kong
- H10N7<sup>3</sup>
  - ◆ Egypt

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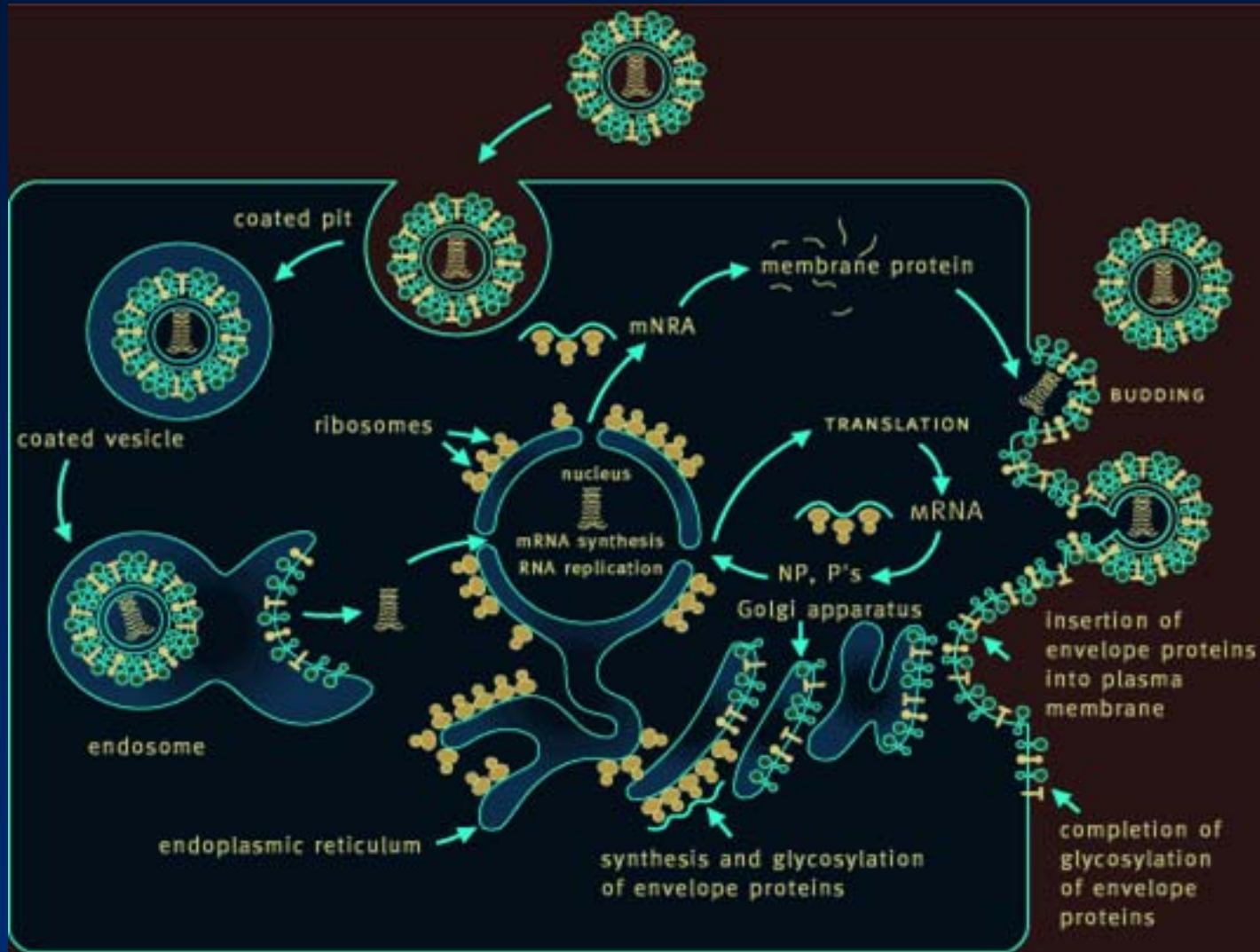
<sup>1</sup> Pan American Health Organization. *EID Weekly Updates*. 2004;2(11).

<sup>2</sup> Pan American Health Organization. *EID Weekly Updates*. 2004;2(2).

<sup>3</sup> Pan American Health Organization. *EID Weekly Updates*. 2004;2(18).



# Replication Cycle Of Influenza Viruses



Lamb RA et al. In: Fields BN et al. eds. *Fields Virology*. 1996, with permission.

# Vaccinology

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## Antigenic Characteristics of Influenza

- Antigenic drift
  - basis of seasonal changes
  - new strains in vaccines from year to year
- Unique antigen types
  - Antibodies may or may not provide cross protection
- Vaccines standardized
  - typically 2 influenza type A and 1 influenza type B
- 2006 – 2007 strains
  - global: H1N1 & H3N2
    - ♦ A/New Caledonia/20/1999 (H1N1)
    - ♦ A/Wisconsin/67/2005 (H3N2)
    - ♦ B/Malaysia/2506/2004

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Centers for Disease Control and Prevention. In: Atkinson W et al, eds. *Epidemiology and Prevention of Vaccine-Preventable Diseases*. 2006.

World Health Organization. Recommendations for Influenza Vaccine Composition. Available at: <http://www.who.int/csr/disease/influenza/vaccinerecommendations1/en/print.html>. Accessed November 8, 2006.

World Health Organization. Influenza. Available at: <http://www.who.int/mediacentre/factsheets/fs211/en/print.html>. Accessed November 8, 2006.

World Health Organization. *Wkly Epidemiol Rec*. 2002;28:229-240.

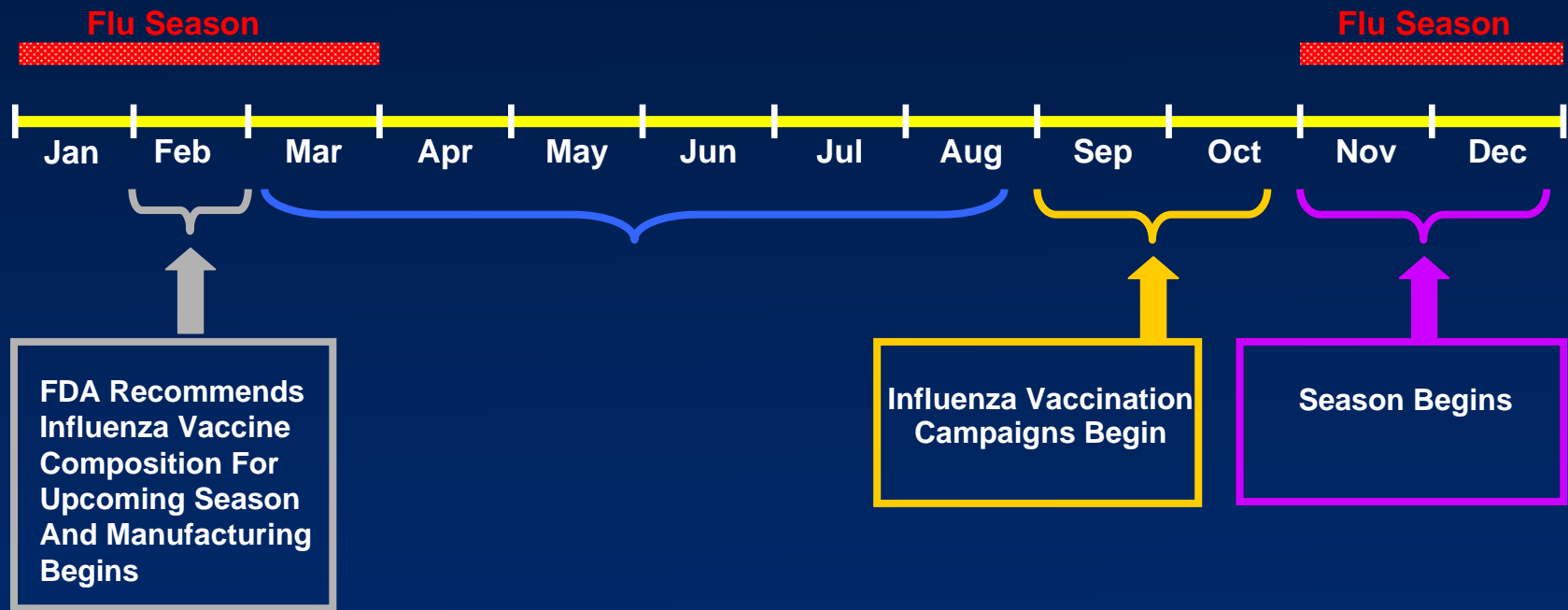
# Vaccinology

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## Correlate of Protection

- Specific hemagglutination-inhibition (HI) titers, post-vaccination with inactivated influenza are not correlated with protection
- HI antibody titers  $\geq 1:40$  have been associated with protection in up to 50%
- Prescribing information no longer using “protection” language

# Influenza Vaccine Development Cycle



Centers for Disease Control and Prevention. *MMWR Morb Mortal Wkly Rep.* 2006;55:1.  
World Health Organization. *Wkly Epidemiol Rec.* 2002;77:229-240.